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THE TERMINATION OF THE NERVES IN THE LIVER.

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As our best histologists have maintained that our knowledge of the termination of the nerves in the liver is very slight and imperfect, I have undertaken, by a careful and extended series of researches, to throw some light on the subject. I have examined livers from the following animals : The dog, cat, woodchuck, owl, crow, hawk, ox and sheep. I have also examined the liver of a child and of an adult. The methods which I have employed have been the simple carmine staining of specimens preserved in chromic acid, picro-carmine, osmic acid, and chloride of gold. None of these reagents proved of much value, except the chloride of gold. The use of osmic acid, so highly praised by some observers, in my hands gave no satisfactory results; for though it makes medullated nerves plainly visible by rendering them black, it has scarcely any effect on non-medullated nerves, and it is these which are to be found in the liver, in a far greater number than medullated nerves. Chloride of gold, as usually employed, also failed to give any good results; but in combination with formic acid it was very satisfactory. The suggestion of a combination of chloride of gold and formic acid I learned from Löwitt;* and my method of employing it was as follows: The liver—best that of man or the ox—is first secured as fresh as possible, frozen by means of the rhigoline spray, in a microtome, and cut into large but very thin sections. It is next placed in a one-half per cent. solution of chloride of gold, and the vessel excluded from the light for thirty to forty minutes. After this it is immediately washed very carefully in distilled water, and at once subjected to formic acid of a specific gravity of 112, from five to eight minutes. The thinner the sections are cut the less time is required for the acid to act upon them. Immediately after their removal from the formic acid they must be again thoroughly washed in distilled water, exposed to the light, and then mounted in glycerine.

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*Löwitt, M. " Die Nerven der Glatten Musculatur," Wiener Akadem, Sitzungs bericht LXXI Bd. Abtheilung Aprilkeft, S. 355.

The place most favorable for finding nerves is, without doubt, the *porta*. In the ox, in the region where the large vessels enter the liver, there is considerable fibrous connective tissue, where numerous bundles of mostly non-medullated nerves may be seen, coursing in the interstices between the bundles. I have succeeded best by taking sections from a portion of the liver immediately bordering on the hepatic artery, a few inches from its entrance into the organ or some of its branches, and so chosen as to include both liver epithelia and connective tissue. I am also of the opinion that the best sections are made by placing the material in the microtome in such a manner that they are cut vertical to the artery.

The nerves were marked by a large number of nuclei, by the presence of a delicate sheath of perineurium around each fibre, and by the dark violet color they had taken on from the treatment before described.

On the border of the lobules the nerves, which were still in bundles of from three to five, and sometimes more, ramified and entered the lobule in different places, mostly branching at acute angles along the capillary blood-vessels. As I have traced the nerves entering the lobule to their connection with the bundles of nerves between the lobules, no doubt can arise as to the nature of the fibres which I have seen. Such fibres are to be found in the interlobular connective tissue, distant from the porta, as well as in the connective tissue of the porta itself. Unquestionable, therefore, the nerves pass into the lobules and ramify along the capillary blood-vessels. This assertion is based on the fact that the ramifying nerves were always seen running in the light interstices between the liver epithelia, which, as we know, are occupied by capillary vessels only.

The further course taken by the nerves can be understood only by considering the fact hitherto unknown to all observers; namely, that the liver epithelia are separated from each other by a delicate layer of cement substance, in the same manner as all other epithelia and endothelia. Our knowledge of this cement substance was first made known by Von D. H. Chr. Müller,* who also claims that it contains excavations from the bile capillaries, which are destitute of walls of their own, and is traversed at right angles by numerous thorns, formerly so-called. The significance of these thorns, according to the views of C. Heitzmann, is plain. The *reticulum* in epithelia of all kinds, was first described by the last-named observer in 1873; and it deserves mentioning that several years later E. Klein, of London, claimed to be the first to describe the reticular structure of the epithelia of the liver. Liver epithelia are in no way different from other epithelia, and it has been proved by the researches of Müller to be composed of living matter, while Klein does not appear to have any idea of its true significance.

The *reticulum* is connected in the center of the epithelium with the walls of the nucleus, and at the periphery with those filaments—also living matter—which penetrate the cement-substance and interconnect all neighboring epithelia. A light rim of this cement-substance is always present between the endothelial wall of the capillaries and the adjacent wall of the epithelium; and again this rim is traversed by delicate grayish filaments, connecting the wall of the capillary with the *reticulum* of living matter in the epithelia. This rim of cement substance proves to be the place where the finest fibrillæ of nerves course. In specimens treated with chloride of gold and formic acid, all structures, except the nerves, were more or less mutilated and rendered indistinct; but, in specimens previously hardened with chromic acid, washed with distilled water, and stained with a one-half per cent. solution of chloride of gold, the relation between epithelia and capillaries is plain. The details can only be seen with high powers (1,000 to 1,200) and excellent immersion lenses. The beaded fibrillæ are connected by means of delicate threads with the walls of the capillary vessel, as well as the threads in the cement substance. Sometimes the nerve-filament is so closely attached to the wall of the epithelium, or to the capillary, or to both of them that the light intervening rim and interconnecting filaments cannot be seen. In other cases the relations are plainly marked. Nerve formations of this description, however, are not very abundant; but this may, perhaps, be owing to an oblique course of the nerve fibers, in consequence of which they are cut across by the razor, and they therefore appear as short threads and mere dots, which cannot be positively recognized as nerves.

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*"Beiträge zur Kenntniss der interstitiellen Leberentzündung." Sitzungsber. der Akademie der Wissenschaften in Wien Bd. LXXIII., 1876.

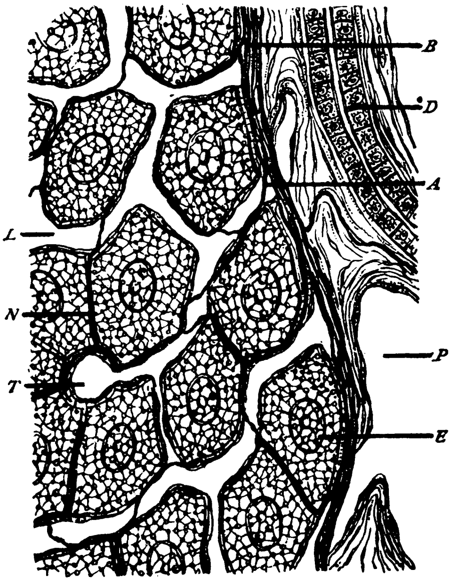

DIAGRAM OF THE TERMINAL NERVE PLEXUS OF THE LIVER.

P.—Portal vein.
D.—Bile-duct.
L.—Capillary vessels in longitudinal section.
T.—Capillary vessels in transverse section.
E.—Liver-epithelia.
B.—Bundle of non-medullated nerve fibres.
A.—Axis-fibrillæ, penetrating the lobules.
N.—Axis-fibrillæ in the cement substance between epithelia.

In the cement substance, between the epithelia, I have sometimes seen delicate filaments around the capillary blood-vessels, which, from analogy, I think I am justified in taking for nerves. These were visible, with high powers, in specimens stained with carmine, but more plainly seen in the specimens stained with chloride of gold.

In none of my large number of specimens have I ever been able to trace a nerve filament penetrating into an epithelium, as is claimed to occur by E. Pflüger. Once or twice I observed a peculiar, pear-shaped enlargement of the nerve, which seemed to be attached to an epithelium, as described by this author; but it was evidently only a swelled nucleus of a non-medullated nerve, having only an apparent, and not a real, attachment, for I saw the same enlargement of the nucleus in the fibrous connective tissue, far away from the epithelia.

It often happens that a large, non-medullated nerve-fiber exhibits an oblong, pear-shaped nucleus-like formation in the axis of the fiber, whose continuity beyond the nucleus is represented by extremely delicate beaded axis-fibrillæ.

My researches are in accordance with those of M. Nesterowsky's assertions, that the blood-vessels of the liver, both the larger vessels of the porta and the capillaries within the lobule of the liver, are accompanied by filaments of nerves. These course in the cement substance (E. Fleischer's connective tissue) between the walls of the capillaries and the epithelia, and also in the cement substance between the neighboring epithelia, without ever entering the borders of the latter. As the filaments traversing the cement substances are formations of living matter, the same as the nerve filaments, and are in connection with the *reticulum* of living matter in the epithelia, we can, I think, understand how nervous impulses may be transmitted from the nerves by these bridges,—the formerly so-called thorns,—directly to the epithelia.

E. Pflüger* first asserted having seen medullated nerve-fibers reaching the surface of the epithelia in the salivary glands and in the liver. According to him, the nerves close to the epithelia lose their myeline investment, and are continued as non-medullated nerves, penetrating the epithelia, and terminating in its nucleus. His assertions, which are repeated in Stricker's "Hand-book of Histology," have not been corroborated by any observer. I must deny the truth of all his assertions concerning the termination of the nerves in the liver.

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*"Nachweis der Nervenendigungen in den Acinösen Drüsen und lin der Leber."—Archiv für Physiologie, S. 50, 1871.

Kupfer* claims to have seen a few nerves enter the epithelia of the ascinous gland, along the œsophagus of the blatta (the cockroach.) As a reagent, he used only the vapor of ammonia.

M. Nesterowsky,† in his very accurate researches, has found the truth, and I coincide with him in his statements, to which I have added a few more facts. This author used the fresh livers of the cat and dog, the blood-vessels of which he injected with colored glue. He used, as a reagent, the chloride of gold, in different degrees of dilution, and afterwards placed the specimens in acetic acid for a few days, adding a drop of ammonia, saturated with sulphuretted hydrogen.

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*"Das Verhältniss von Drüsennerven zu Drüsenzellen."—Archiv für Microscop. Anatomie. Bd. ix., 387, 1873.

†"Ueber die Nerven der Leber."—Virchow's Archiv, 63, Bd. S. 412, 1875.